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Effect of intravenous iron in alleviating symptoms of exhaustion in non-anaemic pre-menopausal women

Submission date 14/02/2010	**Recruitment status** No longer recruiting
Registration date 17/03/2010	**Overall study status** Completed
Last Edited 30/06/2011	**Condition category** Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

N/A

Study information

Scientific Title
Effect of intravenous iron versus placebo on exhaustion symptoms in non-anaemic premenopausal women with low ferritin levels

Acronym
FERRIM

Study objectives
Administration of intravenous iron to non-anemic pre-menopausal women with low serum ferritin (S-ferritin) levels will improve physical and mental performance

Please note that as of 24/05/10 a brief description of the study results has been added to this record. More details are available in the interventions section below.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Both local and central ethical approval was obtained prior to study start - study conducted according to Swissmedic, ICH GCP guidelines and Declaration of Helsinki

Study design
Randomised multicentre double blind placebo controlled superiority study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use contact Lise Riopel [lise.riopel@viforpharma.com] to request a patient information sheet.

Health condition(s) or problem(s) studied
Reduced physical and mental performance in pre-menopausal women

Interventions
Venofer®, (iron sucrose injection) is an aqueous complex of polynuclear iron (III)- hydroxide in sucrose for intravenous use. Patients received either 2 infusions each containing 200 mg iron [III]-

hydroxide sucrose (Venofer®) or 2 infusions of 200 ml 0.9% saline (placebo) administered over a minimum period of 10 minutes each week for the first two weeks of the trial. Each patient received a total of 4 infusions representing a total of 800 mg of iron in the Venofer® treated group. Patients were followed for total period of 3 months.

Added 24/05/10:
Statistical methods:
For description of the distribution medians and range were used. For analysis of differences of distribution of investigated parameters between Venofer and placebo groups, a non parametric test (Mann- Whitney U-Test) was used. Both types of analyses were performed, because deviations from normal distribution were found for primary objective variables, most items are categorically scaled parameters.

Study Results:
1. Efficacy:
Difference from baseline in median Brief Fatigue Inventory (BFI) score between the treatment groups was not statistically significant but suggest a trend toward a greater improvement in patients treated with iron sucrose (difference in change BFI: -0.44, p=0.076). There was a significantly (p=0.036) greater improvement in categorized tBFI scores from baseline to Day 42 in patients treated with IV iron sucrose compared to patients treated with placebo There were significant differences between the study groups in some sub-group analyses. Among patients presenting with severe iron deficiency at baseline (defined as TSAT below 20% and serum ferritin below 50 ng/mL or serum ferritin below 15 ng/mL) there was a significantly greater improvement in BFI score at Day 42, in patients treated with IV iron sucrose compared to patients treated with placebo (p=0.026).
There was a significant correlation between the change in fatigue from baseline to Day 42 as measured by the BFI and the change in fatigue as measured by Short Performance Inventory (SPI), a global investigator assessment (r=0.59, p<0.0001).
Patients treated with IV iron sucrose showed a significant increase in serum-ferritin values during the study compared to baseline, and this increase was significantly greater in the IV iron sucrose group compared to the placebo group (p<0.0001).
The results of this study suggest a clinical benefit for patients treated with iron sucrose and warrant further investigation in this area.

2. Safety:
In total, 54 of 89 enrolled patients reported at least one adverse effect (AE) during the clinical study; most of the AEs were mild and unrelated to study medication. Two serious AEs (SAEs) were reported, one in each treatment group. There was one case of appendicitis and one serious traffic accident. Both were unrelated to treatment. Further, there were no clinically relevant abnormal findings in vital signs, physical exams or evaluation of concomitant medication during the study. This suggests that the iron sucrose treatment caused no safety concerns. It can be concluded that the incidence of AEs following iron sucrose administration is low and reflects the safety profile labelled in the SmPC.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)

Iron [III]-hydroxide sucrose (Venofer®)

Primary outcome measure
1. Brief Fatigue Inventory (total score = tBFI) assessed at baseline, day 42 and 90
2. Serum ferretin, assessed at baseline, 3rd treatment visit, day 42 and 90

Secondary outcome measures
1. BFI intensity mean score and impairment score, assessed at baseline, day 42 and 90
2. Haematological parameters, assessed at baseline, day 42 and 90
2.1. Hb
2.2. Mean corpuscular volume (MCV)
2.3. Mean corpuscular haemoglobin concentration (MCHC)
2.4. Haematocrit (HCT)
3. Iron status, assessed at baseline, 3rd treatment visit, day 42 and 90
3.1. Serum iron
3.2. Transferrin Saturation (Tsat)
3.3. Transferrin
4. Safety
4.1. Adverse effects
4.2. Physical exam, assessed at day 90
4.3. Body weight and height, assessed at day 90
4.4. Vital signs, assessed at baseline, day 42 and 90
4.5. Creatinine, assessed at baseline
4.6. Alanine Aminotransferase (ALT), assessed at baseline
4.7. Aspartate Aminotransferase (AST), assessed at baseline
4.8. C-Reactive protein (CRP), assessed at baseline, day 42 and 90
5. Concomitant medications

Overall study start date
21/09/2006

Completion date
07/08/2008

Eligibility

Key inclusion criteria
1. Premenopausal, regularly menstruating women
2. Age ≥ 18 years
3. S-ferretin < 50ng/mL
4. Signed informed consent
5. Reduced physical and mental performance (fatigue, depressive mood, dizziness, sleep disturbance, concentration, neck pain, headache) as determined by investigator
6. Adequate contraception

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
100 (50 patients/group)

Key exclusion criteria
1. Haemoglobin (Hb) level 120 g/L
2. Known mental and physical disorder (cancer, depression)
3. Use of concomitant medication to cause symptoms of fatigue and depression (antidepressive & chemotherapeutic agents, sedatives)
4. Use of iron preparations within previous 4-weeks
5. Active sever infection, inflammation, malignancy
6. C-Reactive Protein (CRP) > 20 mg/mL
7. Thyroid-Stimulating Hormone (TSH) > 4 micro U/mL
8. Use of menstruation depressing gestagens
9. History of Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV)
10. Significant cardiovascular disease e.g. unstable angina, New York Heart Association (NYHA) class IV
11. Hypersensitivity to iron sucrose or iron sulphate
12. Pregnancy or lactation
13. Participation in any other therapeutic study in the previous month

Date of first enrolment
21/09/2006

Date of final enrolment
07/08/2008

Locations

Countries of recruitment
Switzerland

Study participating centre
Gynakologie Geburtshilfe Seefeld
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CH-8008

Sponsor information

Organisation
Vifor Pharma, Vifor (International) Ltd (Switzerland)

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Vifor Pharma, Vifor (International) Ltd. (Switzerland)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	22/09/2011		Yes	No